79. The method of claim 78, wherein said pH is about pH 6.0.

80. The method of claim 73, wherein said IGF-I is present in said composition at a concentration of about 12 mg/ml to about 200 mg/ml.

81. The method of claim 80, wherein said IGF-I is present in said composition at a concentration of about 15 mg/ml to about 200 mg/ml.

82. The method of claim 81, wherein said IGF-I is present in said composition at a concentration of about 25 mg/ml to about 200 mg/ml.

83. The method of claim 68, wherein said composition comprises sodium chloride at a molar concentration of about 150 mM.

84. The method of claim 68, wherein said composition comprises a buffer selected from the group consisting of a glutaric acid buffer, a maleic acid buffer, a succinic acid buffer, a citric acid buffer, imidazole, and a histidine buffer.

REMARKS

Claims 1-28 have been canceled. Claims 29-84 have been added. Support for the newly added claims resides throughout the specification and in the original claims. No new matter has been added by way of claim amendment. Claims 29-84 are pending in the application. Applicants respectfully request entry of the amendment prior to examination of the present application.

Specifically, claims 1-28 have been canceled. That subject matter encompassed by these claims is now set forth as new claims 29-84. These claims are drawn to compositions having a pH of at least about pH 5.5 and comprising biologically active IGF-I or biologically active analogue thereof (claims 29-48), a method of making these compositions (claims 49-51 and 68-84), a method for enhancing solubility of IGF-I (claims 54-56), and methods for stabilizing solubility (claims 57-60) and biological activity (claims 61-67) of IGF-I. The IGF-I compositions also

comprise a solubilizing compound in an amount sufficient to make the IGF-I soluble at a concentration of at least about 12 mg/ml when the composition is at a temperature of about 4 °C. The IGF-I or analogue thereof in these compositions has an amino acid sequence that shares at least 70% sequence identity with the amino acid sequence for human IGF-I. The solubilizing compound comprises a guanidinium group. Specific solubilizing compounds recited in the claims include guanidine hydrochloride, arginine, or an arginine analogue. Support for these claims resides in the original claims and in the specification. See particularly page 6, lines 7-10, where IGF-I sequences encompassed by the present invention are recited as having an amino acid sequence that shares at least 70% or more sequence identity to the native IGF-I, particularly human IGF-I. Also, see page 7, lines 21-25, where arginine analogues are defined as amino acid analogues of arginine that retain the activity of arginine with regard to the invention, i.e., increasing solubility of IGF-I at pH 5.5 or greater.

No new matter is added by way of claim amendment. The Examiner is respectfully requested to enter the amendment prior to examination of the application.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

David M. Krasnow
Registration No. 34,203

ALSTON & BIRD LLP
P.O. Drawer 34009
Charlotte, NC 28234
Tel Raleigh Office (919) 420-2200
Fax Raleigh Office (919) 420-2260

"Express Mail" Mailing Label Number US
Date of Deposit: December 13, 1999

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Box Patent Application, Assistant Commissioner for Patents, Washington, DC 20231.

Nora Martinez
RTA01/2071231v1